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10/659,566	09/10/2003	Christophe Dupont	2756.001	4677

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EXAMINER	
BETTON, TIMOTHY E	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/659,566	DUPONT ET AL.	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-18* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-12, and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed on 11 December 2008 have been acknowledged and duly made of record.

Claims 1-4, 6, 8, 10-12 and 14-17 have been rejected under 35 USC §103(a) as being unpatentable over Fischer, U.S. Patent No. 4,836,217 ("Fischer"), in view of Antelman, WO/2001/049302 ("Antelman"), Peck, U.S. Patent No. 4,821,733 ("Peck") and Lipper (WO 02/076379 A2).

Applicants' disclose:

We respectfully request reconsideration of the present application, based on the foregoing amendment of the claims and the remarks that follow. In particular, we submit the patch as presently claimed is not obvious over the prior art, which fails to suggest the use of electrostatic forces to maintain an active substance in the form of particles on the surface of a skin patch. As will be discussed below, no prior art references disclosed or suggested a skin patch to directly deliver a substance in its reactogenic state, nor how such a skin patch could be made.

By contrast, the present invention provides for the active substance in the form of individualized or agglomerated dry particles, to be directly maintained on the support by electrostatic forces of attraction between these particles and the support, i.e., without any addition of gel. Skin patches containing an active substance in its reactogenic state of origin (e.g., with no added gel) had never been disclosed or suggested in the art prior to the present invention. Furthermore, it was not known in the art how to make such skin

patches, and the ability to use electrostatic forces according to the present invention was totally unexpected.

Perspiration, which contributes to the electrostatic forces within the dermal patch will naturally form a film. The limitation drawn to free particles is acknowledged but whether it begins in the form of free particles or embedded, electrostatic forces and physiological changes upon the dermis, i.e., temperature and/or perspiration will achieve the same effect therapeutically as being claimed. Thus, the inventive objective of the claimed invention is based upon the configuration of the materials of the skin patch which reasonably acts upon the skin in the same or similar way attributed to skin patches already on the market. In this respect, short of anything in the specification citing a specific distinction as opposed to particles (individualized or agglomerated), it would be obvious in the art to optimize the surface area of any topical medication for greater penetration into the epidermis. This is well-established and art known in the filed of pharmacy technology and biopharmaceutics.

Thus, it would be obvious and practical to apply the active substance as suggested and claimed as distinct in the current invention.

Accordingly, the attached scientific publication by Kalach et al. (JACI 116 (2005) pp1321-1326) and the Declaration of Bertrand Dupont is acknowledged and in light of the response *supra,* it is not found persuasive in view of obviousness to try the optimization of therapeutic effect with a gel or without a gel. Even in the alternative, as applies to the current invention to a general population, it would still be obvious, because of less occlusion and the voidance of buffer-strength attributed to the gel which would

reasonably present a greater chance of greater therapeutic effect via the limitations of the claimed invention.

Applicants' assert [that] the claimed device is not a mere variation of the Finn Chambers. It is a completely novel approach for making patches. The use of an active substance in the form of particles had never been proposed before and represents a very substantial improvement over all prior patch technologies, which used either liquid substances or gels. The use of the substance in the form of a powder increases the stability, avoids denaturation, and allows better dosing. The use of a powder is also much more convenient from an industrial prospective. The ability to use the substance in the form of particles, directly coated and maintained on a support, is in itself unexpected (page 5, last nine lines).

The above does not preclude the claimed limitation of independent claim 1 from being obvious to try. Characterization optimization in order to determine maximum therapeutic efficacy and/or toxicity factors.

In view of applicants' explanation with regard to Antelman, these references are withdrawn from further consideration as will be presented in the following rejection of all claims as currently amended. In the absence of Antelman, the teachings and modifications of Fischer, Peck, and Lipper are sufficient in obviousness over the claimed invention.

Fischer and Lipper are adequate for what they teach in obviousness over the elements in the current invention as disclosed in the last Office action and will be further

elucidated in the following rejection in view of the current response to applicants' arguments above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6, 8, 10-12, and 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer (already incorporated by reference) in view of Peck, U.S. Patent No. 4,821,733.

Fischer teaches a novel device and method for carrying out occlusive epicutaneous tests (patch tests). This type of test is employed for detecting contact allergy to some specific substance (allergen) or for testing allergenic and/or irritant properties of

a substance. The invention is characterized in that the test substance is incorporated in a **dry film** (abstract only).

According to the instant specification, the expression, "electrostatic support" denotes any support made of a material capable of accumulating electrostatic charges and of conserving them by thus, developing maintaining forces, **in particular by rubbing, heating or ionization, or any other technique** (fourth paragraph, pg. 9).

Fischer, in kind, teaches that there are two important steps in the manufacturing procedure which are of prime importance for the result obtained: (1) The test allergen has to be distributed uniformly in the film-forming material. (2) The film carrier has to be coated reproducibly with a film of even thickness. If a hydrophilic vehicle is chosen to be employed on a film carrier which is too hydrophobic in character it may turn out to be difficult to uniformly coat the carrier with the vehicle. In such a case the carrier may be treated so as to be made more hydrophilic. Thus, for instance, a polyester film may be treated for a short period of time in an electric field (e.g. corona discharge treatment), or a polyethylene film may be partially oxidized to introduce polar structures (column 5, lines 43-56).

The above explanation would be recognized by the skilled artisan as an example of electrostatic support according to the definition disclosed in the instant specification.

Fischer teaches a feature of the patch which determines threshold values for a patient by a design of the patch which imparts a different amount/ unit area of the same antigen. Fischer further goes into detail with another limitation of the function of the patch which provides different allergens each, and/or with the same allergen in different

amounts per unit area. By virtue of the varying concentrations and classification of allergen, electrostatic properties would conceivably differ. Thus, Fischer adequately teaches the limitation of claim 12 (col. 6, lines 28-31 and 46-58).

Fischer further teaches the employment of strips as equivalent to other types of patch shapes (see specification, page 17, Conclusion).

Fischer does not teach a method of substantially freeing an active substance of an auxiliary substance when applied topically via dermal patch. Accordingly, the reference to electrostatic properties and forces are not taught expressly by Fischer. However, the electrostatic properties of dermal patches, dressings, band-aids are art known. Any disclosure in the instant claims attributed to electrostatic forces holds no patentable weight in view of this property being a natural chemical reaction due to the hermetic contact of the adhesive of the patch with the skin (col 3, lines 62-68 bridging col. 4, lines 1-4).

Fischer also does expressly teach reasoning drawn to the limitation in the instant claim 1 of a biologically active substance in the absence of added gel, said biologically active substance being in the form of individualized or agglomerated particles. Fischer in the alternate teaches a coalescible emulsion which is not a gel and would readily be incorporated in the absence of gel if at all necessary (col 3, lines 62-68 bridging col. 4, lines 1-4).

Fischer teaches [that] the vehicle will be selected from among substances having film-forming properties. Usually it is a polymer which together with a volatile liquid such as e.g. water will give a gel **or coalescible emulsion in which the test substance chosen can be distributed homogeneously in a dissolved, crystallized, micronized,**

emulsified or dispersed state; in the most practical embodiment of the invention, this polymer is chosen such that its gel or **emulsion** when spread out can dry to form a film. The vehicle should have hydrophilic properties so that it will absorb moisture when in use (col 3, lines 62-68 bridging col. 4, lines 1-4).

Fischer does not describe or disclose other specialized features of a dermal patch as disclosed in claims 10 and 11.

However, Peck teaches a transdermal detection system for the detection of a target substance which migrates to the surface of the skin of a subject by diffusion comprises detector means and attachment means. The detector means includes at least one detector chemical contained in solution and capable of chemically reacting with the target substance as the target substance migrates to the skin surface of the subject to produce a detectable signal, and a barrier means for substantially preventing migration of the detector chemical into the skin surface of the subject. The attachment means maintains the detector means adjacent the surface of the skin of the subject (abstract only).

Peck teaches [that] [t]he detector chemical contained in the detector means is capable of chemically reacting with the target substance as the target substance migrates to the surface of the skin of the subject to produce a detectable signal. The detectable signal which results may be, for example, an optically detectable signal such as a visible color change or an electrically detectable signal such as a change in pH, i.e. a change in the hydrogen ion concentration, or other ion concentrations change. Other optically and electrically detectable signals which may result from the chemical reaction of the detector

chemical with the target substance will be apparent to one skilled in the art and are included within the scope of the present invention (column 4, lines 1-14).

Claim 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer and Peck, U.S. Patent No. 4,821,733 as applied to claims 1-6 ,8, 10-12 and 14-17 above, and further in view of Lipper et al. (WO 02/076379 A2).

Lipper et al. teach a medicated tattoo [which]comprises a section of cardstock base paper (70), clear base (50) having an ink design on one side and attached to (70) on the other side by a release base (60) which dissolves when wet to allow detachment of (70); an adhesive layer (20) coated over the ink design on (50) for adhesion to the skin; and a medicament incorporated in the adhesive layer for diffusion into the skin of the wearer. The adhesive layer is formed with one from micropores and microchannels having pre-determined permeability characteristics (abstract only).

Also, Lipper et al. teach [that] the tattoo further comprises a permeable membrane between the drug substance layer and (200) for controlling desorption of the medicament through (20). The tattoo further comprises an indicator dye incorporated into the drug substance layer which migrates with the medicament **to indicate progress or which changes over time to indicate useful life; or a layer incorporated into the drug substance layer and visible in conjugation with the colored design layer to provide a color-changing design as a child incentive to wear** (page 18).

Thus, it would have been prima facie obvious to the one of skill at the time of invention to at once recognize a reasonable expectation of success via the combining and incorporating together the teachings and methods of Fischer, Peck and Lipper.

The differences between the prior art and the claims at issue are the limitations of claims 2 and 4 which are drawn to common and normal features of most dermal patches, transdermal patches, band-aids, etc. The limitations of claims 2 and 4 are normal functional attributes of a dermal patch.

Considering objective evidence present in the application indicating obviousness or nonobviousness, atopy patches are well-known in the art. Variations and variable constructions of such patches make the claimed invention obvious. The teachings of Fischer principally, disclose art that encompasses the inventive objective of the claimed invention. Fischer also discloses the suggestion that gel does not have to be incorporated into the patch. Instant claim 1 discloses the open-ended term *comprising* which reasonably suggests the propensity for the use of other vehicles or the absence thereof. **The claimed invention discloses nothing in the current claims suggesting the absence of a film-forming substance. However, in the total absence of a gel, film-forming would still occur due to naturally occurring temperature and physiological changes on the epidermis, e.g., perspiration.**

Specifically, the instant specification does not reasonably suggest that the invention as disclosed has the absence of film-forming.

Peck teaches a colored indicator sensitive to local variations of pH which the one of skill would deem reasonable to incorporate into the teachings of Fischer and further in Lipper. Lipper teaches the use of a tattoo patch, which is not only medicated but also serves as an indicator dye to monitor the progression of the active agent. The references cited above all teach the administration of a dermal patch. **Again, the one of skill would be inclined to incorporate these references together because the Fischer reference provides the inventive objective by which the references that follow teach reasonable features to improve therapeutic efficacy**. Also, reasonably the one of skill would instantly recognize that the references overlap as far as the device implemented for therapeutic administration. The references complement one another in that particularly the improvements of Peck and Lipper in view of the claimed invention are improvements which reasonably flow with the course of the claimed invention.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 2729922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617